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Docket No.: 242/9-1568

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Roberto Valducci  
Serial No.: 09/898,425 Group Art Unit: 1615  
Filing Date: July 3, 2001 Examiner: Blessing M. Fubara  
For: ORAL SOLID PHARMACEUTICAL FORMULATION WITH PH-  
DEPENDENT MULTIPHASIC RELEASE

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Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**RESPONSE TO FINAL OFFICE ACTION**

Sir:

In response to the Final Office Action dated January 11, 2005, the applicant respectfully traverses the examiners' grounds for rejection.

Claims 35 and 37-46 have been rejected under 35 U.S.C. 103(a) as being obvious over Hirakawa et al in view of Khan et al.

The examiner has failed to appreciate what the references truly describe and failed to give proper weight to the specific limitations of claim 35.

The examiner states that "the Khan coated layer disintegrates at different pHs. Specifically, Table 1, page 218, formulation 3:2 at level 13.9 disintegrates at pH of 6.0, 6.5, 6.8 and 7.0." However, that the coating dissolves at different pH levels is of little relevance, as it is the pH at which the coating begins to dissolve that is relevant to claim 1.

Claim 1 requires a "formulation having at least three coated active ingredient portions, a first portion having a coating soluble starting from a pH of 6, a second portion having a coating

soluble starting from a pH of 6.5 and a third portion having a coating soluble starting from a pH of 7".

The examiner should agree that the Khan 3:2 formulation referenced above has only one starting solubility, relative to increasing pH, specifically starting at 6.0. Each formulation of Table 1 has only one pH at which significant dissolution begins. This can be identified from top to bottom with increasing pH, the last entry for the 0:1 formulation dissolving at a pH of 7.5.

Nowhere in Khan is there a teaching or suggestion for a multiphasic release formulation comprised of at least three coated active ingredient portions, having coatings with different initial solubility.

Hirakawa also does not teach or suggest the dividing of an active ingredient into a plurality of portions, each portion receiving its own coating for initial dissolution at different pH values corresponding to different areas of the GI tract. Hirakawa relies on mechanical pressing as increasing acid resistance. Examples 1-5 all describe a single active core tablet that is "press-coated", that is, there is only a single active ingredient portion, coated for initial release of the active ingredient at a single pH. While the press coating can have multiple layers, together they form only one coating of the active ingredient, and the active cannot be released till the entire coating has been penetrated. The multiple layers act in the same way as the increased coating thickness in Khan Table 1, to delay the initial release of the active. This is nothing like the claimed invention.

As described above, Khan seeks a "single coating system for colon targeted oral delivery of drugs" (P. 216). Hirakawa also seeks only a single coating, but one that is applied by pressing. Such single coating systems does not teach or suggest the separation of an active ingredient into discrete portions, each portion having a coating that initially dissolves at a pH different from the

other portions.

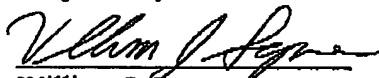
To establish a prima facie case of obviousness based on a combination of references, there must be some teaching, suggestion or motivation in the prior art to make the specific combination that was made by the applicant. In re Raynes, 7 F.3d 1037, 1039, 28 U.S.P.Q.2D (BNA) 1630, 1631 (Fed. Cir. 1993); In re Oetiker, 977 F.2d 1443, 1445, 24 U.S.P.Q.2D (BNA) 1443, 1445 (Fed. Cir. 1992). Obviousness can not be established by hindsight combination to produce the claimed invention. In re Gorman, 933 F.2d 982, 986, 18 U.S.P.Q.2D (BNA) 1885, 1888 (Fed. Cir. 1991). As discussed in Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1143, 227 U.S.P.Q. (BNA) 543, 551 (Fed. Cir. 1985), it is the prior art itself, and not the applicant's achievement, that must establish the obviousness of the combination.

Here, only the applicant's disclosure has the teaching for the invention of claim 35, and the examiner has engaged in a hindsight reconstruction not taught or suggested by the prior art. Given a fair reading of the references as a whole, claims 35 and 37-46 are unobvious and withdrawal of the rejection is respectfully requested.

Based on the above remarks, favorable consideration and allowance of the application is respectfully requested. However should the examiner believe that direct contact with the applicant's attorney would advance the prosecution of the application, the examiner is invited to telephone the undersigned at the number given below.

Coleman Sudol Sapone P.C.  
714 Colorado Avenue  
Bridgeport, CT 06605  
Telephone No. (203) 366-3560  
Facsimile No. (203) 335-6779

Respectfully submitted,

  
William J. Sapone  
Registration No. 32,518  
Attorney for Applicant(s)